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09/616,787	07/14/2000	David F. Englert	10296-050001	6941

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EXAMINER	
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ART UNIT	PAPER NUMBER
1634	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/616,787	Englert
Examiner	**Art Unit**
Arun Chakrabarti	1655

-- **The MAILING DATE of this communication appears on the cover sheet with the correspondence address** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Feb 11, 2002 .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-6 and 36-41 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-6 and 36-41 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Specification

1. Claim 1 has been amended and new claims 36-41 have been added.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

3. Claims 1-5 and 36 are rejected under 35 U.S.C. 102 (e) as being anticipated by Wong (U.S. Patent 5,935,793) (August 10, 1999).

Wong inherently teaches a method for multiplexed analysis of a plurality of target nucleic acid sequences in a sample (Abstract) comprising the methods of:

providing, for each target nucleic acid sequence to be analyzed, at least one probe/primer molecule which probe/primer molecule includes a region of sequence substantially complementary to a sequence in the target nucleic acid sequence and a region that is not located at either terminus of the probe/primer and which includes a capture tag sequence (Abstract and Figures 1A and 1B and Column 5, line 49 to column 6, line 7 and Tables 1-3);

forming a reaction mixture which includes the probe/primer molecules and the target sequences under conditions such that, if a probe/primer molecule specific for a target sequence and the target sequences are both present, one or a plurality of derivative molecules having a capture tag at one or both its 3' or 5' termini, of the probe specific for the target sequence, is generated, and evaluating the presence of one or more derivative molecules, each derivative molecule indicating a target nucleic acid sequence in the sample, thereby analyzing the plurality of target nucleic acid sequences in the sample (Figure 4 and Examples 1 and 2 and Column 12, line 6 to column 14, line 12);

evaluating the presence of one or more capture sequence tags (Figure 5 and Column 20, lines 47-60).

Wong teaches a method wherein the derivative nucleic acid molecules are analyzed by hybridizing the tag sequences to capture probes which are spatially separated (Figure 4 and Examples 1 and 2).

Wong inherently teaches a method wherein the capture probes are partially duplex probes with capture-tag-complementary single stranded overhangs (Table 2 and Column 24, lines 24-30).

Wong teaches a method wherein the capture tags are disposed on beads (Column 22, lines 7-12).

Wong teaches a method wherein the capture tags are disposed on an ordered array (Figures 3-5 and Examples 1-2).

Wong teaches a method wherein the probe/primer molecule comprises a restriction endonuclease recognition site (Column 12, lines 6-12 and Column 14, lines 3-12).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-6 and 36 are rejected under 35 U.S.C. 103 (a) over Wong (U.S. Patent 5,935,793) (August 10, 1999) in view of Zhang et al. (U.S. Patent 5,942,391) (August 24, 1991).

Wong teaches the methods of claims 1-5 and 36 as described above.

Wong does not teach the method wherein the derivative nucleic acid is ligated to a capture probe and then washed.

Zhang et al. teach the method wherein the derivative nucleic acid is washed and then ligated to a capture probe. (Column 40, lines 1-27 and Figure 5). However, MPEP 2144.04 further states, " *In re Gibson,* 39 F.2d 975, 5 USPQ 230 (CCPA 1930) Selection of any order of mixing ingredients is *prima facie* obvious".

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the washing and ligation steps of Zhang et al. into the method of Wong, since Zhang et al. state, "The beads were then washed twice with

washing buffer to remove nonhybridized probes, as well as GnSCN, proteins, nucleic acids, and any potential PCR inhibitors (Column 40, lines 4-8)." By employing scientific reasoning, an ordinary artisan would have combined and substituted the washing and ligation steps of Zhang et al. into the method of Wong in order to improve the analysis of a plurality of target nucleic acid. An ordinary practitioner would have been motivated to combine and substitute the washing and ligation steps of Zhang et al. into the method of Wong, in order to achieve the express advantages noted by Zhang et al., of a method that provides removal of nonhybridized probes, as well as GnSCN, proteins, nucleic acids, and any potential PCR inhibitors.

6. Claims 1-5 and 36-40 are rejected under 35 U.S.C. 103 (a) over Wong (U.S. Patent 5,935,793) (August 10, 1999) in view of Sorge et al. (U.S. Patent 6,261,797 B1) (July 17, 2001).

Wong teaches the methods of claims 1-5 and 36 as described above.

Wong does not teach the method wherein the cleavage of the probe/primer molecule with the restriction endonuclease leaves the capture tag sequence in a single-stranded overhang.

Sorge et al teach the method wherein the cleavage of the probe/primer molecule with the restriction endonuclease leaves the capture tag sequence in a single-stranded overhang (Column 7, lines 6-25)

Wong does not teach the method wherein the endonuclease recognition site is a Type IIS restriction endonuclease recognition site.

Sorge et al teach the method wherein the endonuclease recognition site is a Type IIS restriction endonuclease recognition site.(Column 5, line 5 to column 6, line 48).

Wong does not teach the method wherein the forming comprises cleaving probe/primer molecules that are annealed to target sequences with a Type IIS restriction endonuclease.

Sorge et al teach the method wherein the forming comprises cleaving probe/primer molecules that are annealed to target sequences with a Type IIS restriction endonuclease.(Column 5, line 5 to column 6, line 48)

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method wherein the endonuclease recognition site is a Type IIS restriction endonuclease recognition site of Sorge et al. into the method of Wong, since Sorge et al. state, "Particularly preferred are sites recognized by Type IIS restriction endonucleases. When these primers are used to amplify a polynucleotide product, and then treated with Type IIS restriction endonucleases, the polynucleotide sequence in the synthesized product which comprise the type IIS recognition sequence are completely or partially removed. Thus, using the methods of the invention, one may efficiently synthesize and manipulate polynucleotides of interest by primer mediated polynucleotide synthesis, e.g., PCR, without introducing some or all of the primer-derived nucleotides into the ultimate synthesis products (Column 5, lines 15-26)." By employing scientific reasoning, an ordinary artisan would have combined and substituted the method wherein the endonuclease recognition site is a Type IIS restriction endonuclease recognition site of Sorge et al. into the method of Wong, in order to improve the analysis of a plurality of target nucleic acid. An ordinary practitioner would have been motivated to combine and substitute the method wherein the endonuclease recognition site

is a Type IIS restriction endonuclease recognition site of Sorge et al. into the method of Wong, in order to achieve the express advantages noted by Sorge et al., of an invention that provides particularly preferred sites recognized by Type IIS restriction endonucleases and the methods by which one may efficiently synthesize and manipulate polynucleotides of interest by primer mediated polynucleotide synthesis, e.g., PCR, without introducing some or all of the primer-derived nucleotides into the ultimate synthesis products.

7. Claims 1-5, 36, and 41 are rejected under 35 U.S.C. 103 (a) over Wong (U.S. Patent 5,935,793) (August 10, 1999) in view of Matsui et al. (U.S. Patent 6,255,081 B1) (July 3, 2001).

Wong teaches the methods of claims 1-5 and 36 as described above.

Wong does not teach the method wherein the forming comprises cleaving probe/primer molecules with a flap endonuclease.

Matsui et al. teach the method wherein the forming comprises cleaving probe/primer molecules with a flap endonuclease (Abstract, Claims 1-8, and Examples 6-9).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method wherein the forming comprises cleaving probe/primer molecules with a flap endonuclease of Matsui et al. into the method of Wong, since Matsui et al. state, "Further, this enzyme is thermally stable, so it becomes possible to develop new techniques of conducting artificial homologous recombination of genetic shuffling highly efficiently by coupling the enzyme reaction with PCR (Abstract, last sentence)." By employing scientific reasoning, an ordinary artisan would have combined and substituted the

method wherein the forming comprises cleaving probe/primer molecules with a flap endonuclease of Matsui et al. into the method of Wong in order to improve the analysis of a plurality of target nucleic acid. An ordinary practitioner would have been motivated to combine and substitute the method wherein the forming comprises cleaving probe/primer molecules with a flap endonuclease of Matsui et al. into the method of Wong, in order to achieve the express advantages noted by Matsui et al., of a thermally stable enzyme, so that it becomes possible to develop new techniques of conducting artificial homologous recombination of genetic shuffling highly efficiently by coupling the enzyme reaction with PCR.

Response to Amendment

8. In response to amendment, 112 (second paragraph) rejection has been withdrawn. However, 102 (e) rejection and 103 (a) rejection have been maintained. Two new 103 (a) rejections have been included.

Response to Arguments

9. Applicant's arguments filed on February 11, 2002, have been fully considered but they are not persuasive.

Applicant argues that Wong reference does not teach the probe/primer of the claimed invention. Applicant argues that the word "modifying" or "cleaving" the tag by restriction endonuclease was not found in Wong reference and only the word "primer-tag-primer" or "tag-primer" are found. Applicant argues that because Wong has a preferred embodiment of "primer-

tag-primer" or "tag-primer", Wong is limited to the preferred embodiment. This argument is not persuasive. As MPEP 2123 states "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi,169 USPQ 423 (CCPA 1971)." MPEP 2123 also states " A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories , 10 USPQ2d 1843 (Fed. Cir. 1989)." It is clear that simply because Wong has a preferred embodiment, this embodiment does not prevent the reference from suggesting broader embodiments in the disclosure and that this does not constitute a teaching away. Although Wong reference uses "primer-tag-primer" or "tag-primer", the property of being modified and cleaved is inherently present in this chemically and structurally identical molecule. For example, Wong teaches that such "primer-tag-primer" or "tag-primer", can be subjected to modification and cleaving by restriction endonuclease (Column 12, line 6 to column 14, line 12). Moreover, MPEP 2111 states, "Claims must be given their broadest reasonable interpretation. During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification". Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than it is justified. *In re Prater,* 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969)".

Applicant's arguments with respect to new claims 36-41 have been considered but are moot in view of the new ground(s) of rejection (two new 103 (a) rejections). Therefore, all the

rejections made in the first office action is hereby maintained along with two new 103 (a) rejections.

Conclusion

10. **THIS ACTION IS MADE FINAL in view of the response to argument and new ground of rejections as necessitated by the amendment.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Arun Chakrabarti,

Patent Examiner,

February 19, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600